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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 5 :
A61K 31/715, 9/14

A1

(11) International Publication Number: WO 91/10434

(43) International Publication Date: 25 July 1991 (25.07.91)

(21) International Application Number: PCT/GB91/00018

(22) International Filing Date: 7 January 1991 (07.01.91)

(30) Priority data:
9000459.9 9 January 1990 (09.01.90) GB

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(81) Designated States: AT (European patent), AU, BE (European patent), BR, CA, CH (European patent), DE (European patent), DK (European patent), ES (European patent), FR (European patent), GB (European patent), GR (European patent), IT (European patent), JP, KR, LU (European patent), NL (European patent), NO, SE (European patent), US.

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: A MEDICAMENT COMPRISING METHYLCELLULOSE OR HYDROXYALKYL METHYLCELLULOSE, AND USE THEREOF

(57) Abstract

Methylcellulose or hydroxyalkyl methylcellulose is used in a therapeutic method involving protecting sensitized nerve endings from over stimulation, and particularly in the treatment by nasal administration of allergies and other conditions caused by inhalation of airborne irritants. The medicament forms a gel which protects the disturbed nerve endings long enough for them to return to their normal sensitivity. The medicament is quick-acting and straightforward to use, and does not have undesirable side effects.

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A medicament comprising methylcellulose or hydroxyalkyl methylcellulose, and use thereof.

This invention relates to medicaments for therapeutic treatments, such as treatments for protecting sensitized nerve endings from over stimulation, and is more particularly, but not exclusively, concerned with treatment of allergies and other conditions caused by inhalation of airborne irritants.

Many people suffer to a greater or lesser extent from the effects of allergies due to inhalation of airborne irritants, such as pollen or household dust.

The effects of an allergy to pollens are commonly styled "hay fever" (Allergic Rhinitis), and can lead to sneezing, catarrh and conjunctivitis amongst other symptoms. Known methods of treatment of hay fever are not always reliable and can give rise to undesirable side effects, such as drowsiness.

It is an object of the invention to provide a medicament for treatment of such allergies and other respiratory complaints which is straightforward to use and does not have undesirable side effects.

According to one aspect of the invention there is provided a medicament comprising methylcellulose or hydroxyalkyl methylcellulose for use as an active ingredient in a therapeutic method.

According to another aspect of the present invention there is provided a medicament comprising methylcellulose or hydroxyalkyl methylcellulose for use in

the treatment by nasal administration of allergies and other conditions caused by inhalation of airborne irritants.

According to another aspect of the invention there is provided the use of methylcellulose or hydroxyalkyl methylcellulose for the preparation of a medicament for use as an active ingredient in a therapeutic method involving protecting sensitized nerve endings from over stimulation.

According to a further aspect of the present invention, there is provided the use of methylcellulose or hydroxyalkyl methylcellulose for the preparation of a medicament for use in the treatment by nasal administration of allergies and other conditions caused by inhalation of airborne irritants.

The methylcellulose or hydroxyalkyl methylcellulose may be in powder, liquid or gel form, and may be in the form of hydroxypropyl methylcellulose, hydroxyethyl methylcellulose, hydroxymethyl methylcellulose or hydroxybutyl methylcellulose.

In such an application, where the methylcellulose or hydroxyalkyl methylcellulose is in the form of a powder, it is important that the powder has effective particle sizes acceptable to the nose and preferably less than about 50 microns diameter (or about 25 microns diameter in some circumstances). Typically at least about 90% by weight of the powder will consist of particles having effective particle diameters in the range

of about 5 to about 50 microns, and preferably in the range of about 10 to about 40 microns.

The use of hydroxypropyl methylcellulose as a thickener and suspending agent in the pharmaceutical and food industries is well known. It is also used as a tablet binder and in ophthalmic preparations (see Martindale, The Extra Pharmacopeia, 28th Edition, page 956). However, so far as the Applicant is aware, there has been no previous suggestion to use this substance as the therapeutic component of a medicament for use in desensitizing over-sensitized nerve endings, or more specifically in the treatment by nasal administration of allergies and other conditions caused by inhalation of airborne irritants.

The medicament of the invention is capable of broad application to humans or animals in the treatment of respiratory problems, including pneumoconiosis and asthma, as well as in other applications in which sensitized nerve endings are to be protected from over stimulation. In certain of these applications it may be appropriate for the medicament to be orally inhaled or swallowed, or for the medicament to be in the form of a gel.

The invention also provides a delivery system for a medicament for use as an active ingredient in a therapeutic method, the system comprising a container for the medicament, sealing means for closing off the container, and open cell foam means within the container for holding medicament in such a manner as to enable a

quantity of the medicament held within the foam means to be inhaled through the user's nose or otherwise administered to the user.

In one embodiment the container is a flexible strip having a pocket containing the foam means and having an opening to the pocket in one face, and the sealing means is a piece of adhesive tape which closes off the opening.

In another embodiment the container is a receptacle having a top and having a pad of foam means at its top so that the foam means may be charged with medicament by turning the receptacle upside down, and the sealing means is a detachable cap which closes off the top of the receptacle including the foam means.

In this case the receptacle preferably has flexible walls so as to permit the receptacle to be squeezed to assist inhalation of medicament.

In order that the invention may be more fully understood, reference will now be made, by way of example, with reference to the accompanying drawing, in which:

Figure 1 is a schematic view of a delivery system for the medicament in accordance with the invention;

Figure 2 is a section through an alternative delivery system for the medicament in accordance with the invention.

In one form of the invention, hydroxypropyl methylcellulose powder is taken by the user in the manner

of snuff. The hydroxypropyl methylcellulose powder is produced from the cellulose fibres of cotton linters or wood pulp with hydroxypropyl substitution on the anhydroglucose unit being introduced during manufacture. An appropriate powder is that sold under the Registered Trade Mark, Methocel. Such a powder conforms to U.S.P., Food Chemicals Codex, Kosher Certification and F.D.A. regulations.

Whilst various grades of hydroxypropyl methylcellulose powder may be used, it is much preferred that a grade of powder should be used which has a nominal viscosity in a 2% aqueous solution close to that of mucus, and typically in a range of 4000 to 100000 cP at 20° C (although it is preferable that this value is greater than 6000, and most preferably greater than 8000, and/or that this value is less than 50000, and most preferably less than 30000). The powder should also have a high hydration rate so that it will form a gel in a short period of time, typically 3 to 5 seconds, on contact with warm, damp air. A preferred grade of Methocel powder is that sold as K15M Premium which has a nominal viscosity of 15000 cP in 2% aqueous solution at 20° C.

When inhaled the powder acts as a "chemical bandage" to protect sensitized nerve endings within the nose or throat from over stimulation by inhaled irritants. It does this because the powder turns to a gel on contact with the moisture naturally present in the nasal passages. This gently protects the disturbed nerve endings long

enough for them to return to their normal sensitivity. The powder disperses after a while, and is absorbed by the body without any adverse affect. Under most conditions it should not be necessary to administer the powder more than once or twice a day.

If required the powder can be used as a carrier for carrying any suitable drug, for use in treatment of asthma, for example, to the respiratory tract, or elsewhere in the body, and for holding the drug in the required location.

Whilst the powder can be taken simply in the manner of snuff without requiring a special delivery system, it is preferred that the powder is applied and administered by a special delivery system which ensures that the correct amount of powder is taken in a particularly reliable manner.

Figure 1 shows a delivery system 1 in the form of a flexible and transparent plastics strip 2 formed by heat welding together two plastics sheets along weld lines 3, 4 and 5 so as to form a pocket 6 for a pad 7 of open cell foam containing the powder. A circular opening 8 is provided in one of the plastics sheets to provide access to the pocket 6, and this opening 8 is closed off by a piece 9 of adhesive tape (shown in broken lines) applied to one face of the strip 2 when the delivery system 1 is supplied for use.

In use of the delivery system 1 of Figure 1, the piece 9 of adhesive tape is removed so as to provide

access to the powder in the foam pad 7 by way of the opening 8 to permit the powder to be delivered to the user's nose or mouth. The strip 2 is then held by the user grasping each end of the strip 2 between the thumb and forefinger of each hand, and positioned so that the opening 8 is immediately beneath one nostril. The required amount of powder is then taken up by a gentle sniff, and the procedure is repeated for the other nostril. The delivery system 1 is then disposed of.

Figure 2 shows an alternative delivery system 10 in which a quantity of powder 11 sufficient for a number of doses is held within a tubular receptacle 12 made of flexible plastics material. The receptacle 12 is formed at its top with a first screwthread 13 for receiving a detachable screwthreaded cap 14, and a second screwthread 15 for receiving a screwthreaded foam pad holder 16. The pad holder 16 comprises a screwthreaded collar 17, an open cell foam pad 18 and an apertured domed member 19. The form of the apertures in the domed member 19 is shown in the view from below of the member 19 at (a) in Figure 2. The foam pad 18 is held at its periphery between an outer circular flange 20 of the domed member 19 and an inner circular flange 21 of the collar 17. Furthermore the flange 20 of the domed member 19 is trapped in position when the collar 17 is held in screwthreaded engagement with the top of the receptacle 12.

In use of the delivery system 10, the receptacle 12 is turned upside down to charge the foam pad 18 with

powder. The receptacle 12 is then turned upright and the cap 14 is removed by unscrewing it from the receptacle 12. After the user has gently blown his nose, he then places the foam pad 18 on top of the receptacle 12 immediately below one nostril and lightly sniffs the pad 18 so as to inhale the powder, whilst squeezing the walls of the flexible receptacle 12. The procedure is then repeated for the second nostril, and the cap 14 is subsequently replaced, the receptacle 12 being stored for further use.

Whilst the description of the medicament above is concerned with inhalation of the powder for treatment of airborne allergies, it should be appreciated that the medicament can also be used as a "chemical bandage" in other applications within the scope of the invention. For example, the medicament may be applied in the form of a powder or liquid to tissue during surgery so that it will form a "chemical bandage" preventing undesirable cohesion of tissue after surgery.

CLAIMS

1. A medicament comprising methylcellulose or hydroxyalkyl methylcellulose as an active ingredient in a therapeutic method.

2. A medicament comprising methylcellulose or hydroxyalkyl methylcellulose for use in the treatment by nasal administration of allergies and other conditions caused by inhalation of airborne irritants.

3. A medicament according to claim 1 or 2, which is in powder form.

4. A medicament according to claim 3, wherein the powder has effective particle sizes in the range of 0.25 to 25 microns.

5. A medicament according to any preceding claim, which is selected from the group comprising hydroxypropyl methylcellulose, hydroxyethyl methylcellulose, hydroxymethyl methylcellulose and hydroxybutyl methylcellulose.

6. The use of methylcellulose or hydroxyalkyl methylcellulose for the preparation of a medicament for use as an active ingredient in a therapeutic method involving protecting sensitized nerve endings from over stimulation.

7. The use of methylcellulose or hydroxyalkyl methylcellulose for the preparation of a medicament for use in the treatment by nasal administration of allergies and other conditions caused by inhalation of airborne irritants.

8. The use according to claim 6 or 7, wherein the medicament is in powder form.

9. The use according to claim 8, wherein the powder has effective particle sizes in the range of 0.25 to 25 microns.

10. The use according to any one of claims 6 to 9, wherein the medicament is selected from the group comprising hydroxypropyl methylcellulose, hydroxyethyl methylcellulose, hydroxymethyl methylcellulose and hydroxybutyl methylcellulose.

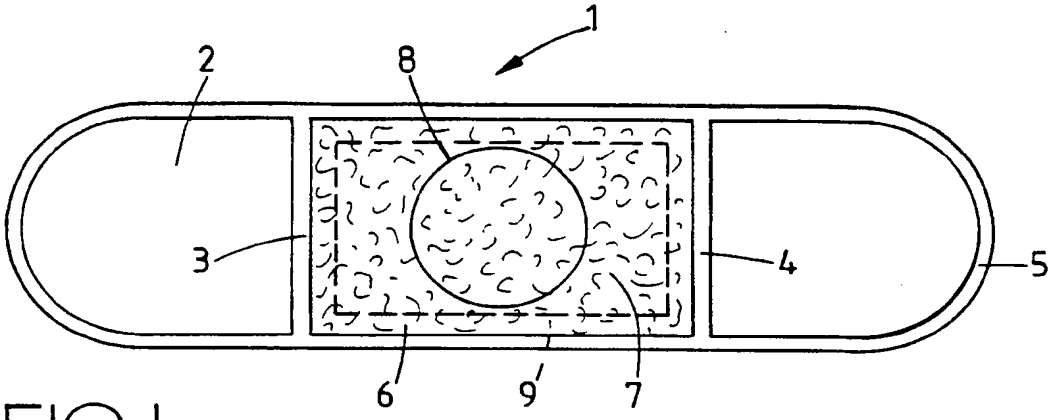

FIG. 1.

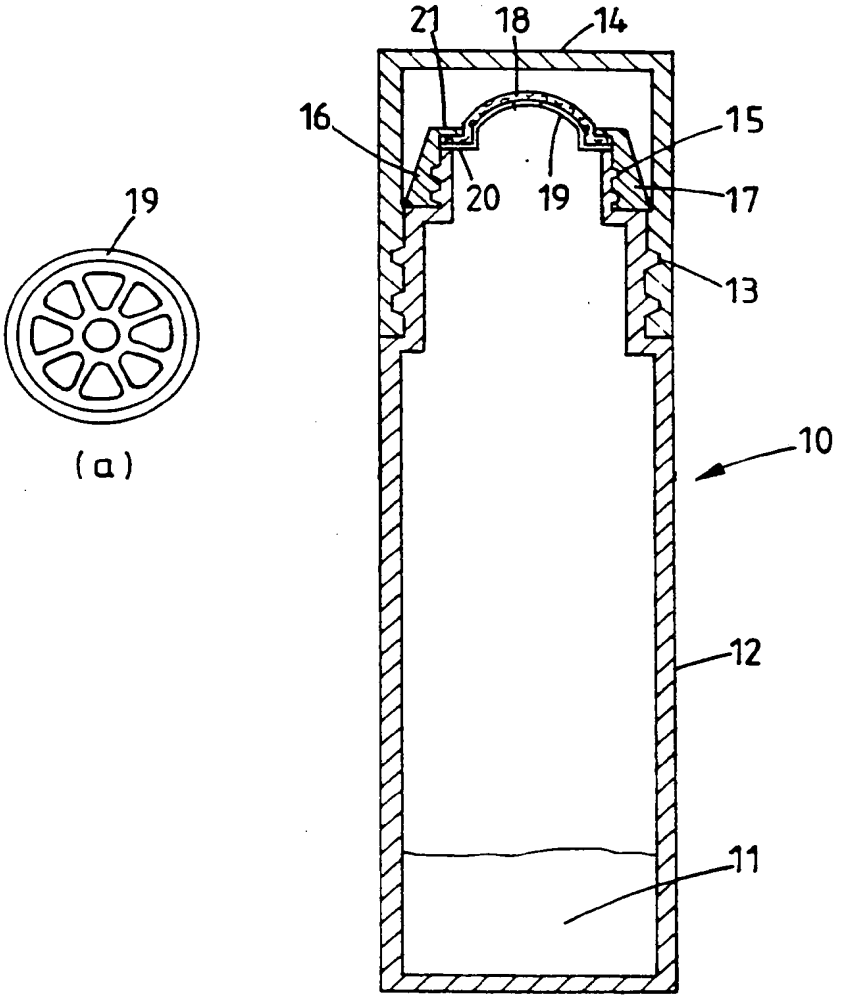

FIG. 2.

INTERNATIONAL SEARCH REPORT

International Application No PCT/GB 91/00018

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [6]

According to International Patent Classification (IPC) or to both National Classification and IPC

IPC[5]: A 61 K 31/715, A 61 K 9/14

II. FIELDS SEARCHED

Minimum Documentation Searched [7]

Classification System	Classification Symbols
IPC[5]	A 61 K

Documentation Searched other than Minimum Documentation to the Extent that such Documents are included in the Fields Searched [8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT [9]

Category *	Citation of Document, [11] with indication, where appropriate, of the relevant passages [12]	Relevant to Claim No. [13]
X	Chemical Abstracts, vol. 99, no. 21, 21 November 1983, (Columbus, Ohio, US), see page 75, abstract 169528h, & JP, A, 58135805 (TEIJIN LTD) 12 August 1983 --	1-10
X	FR, A, 2085692 (SQUIBB) 31 December 1971 see the whole document; especially claims 1-3,7; page 1, line 24 - page 2, line 8	1,2
A	--	3-5
A	EP, A, 0193372 (TEIJIN) 3 September 1986 see the whole document ----------	1-5

* Special categories of cited documents: [10]

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
20th March 1991	27 MAY 1991
International Searching Authority	**Signature of Authorized Officer**
EUROPEAN PATENT OFFICE	MISS D. S[illegible]

Form PCT/ISA/210 (second sheet) (January 1985)

FURTHER INFORMATION CONTINUED FROM THE SECOND SHEET

V. [X] OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND partially unsearchable

This international search report has not been established in respect of certain claims under Article 17(2) (a) for the following reasons:

1. [ ] Claim numbers ..... because they relate to subject matter not required to be searched by this Authority, namely:

2. [X] Claim numbers 2,6,7 because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

It is not clear which diseases are meant by "... other conditions ..." (claims 2,7) and "... involving protecting sensitized narve endings..." (claim 6) (art. 6 PCT). The search has therefore been carried out on the diseases mentioned in the description, ie rhinitis, allergy, asthma, hay fever and pneumoconiosis

3. [ ] Claim numbers....., because they are dependent claims and are not drafted in accordance with the second and third sentences of PCT Rule 6.4(a).

VI. [ ] OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING [2]

This International Searching Authority found multiple inventions in this international application as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims of the international application.

2. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims of the international application for which fees were paid, specifically claims:

3. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim numbers:

4. [ ] As all searchable claims could be searched without effort justifying an additional fee, the International Searching Authority did not invite payment of any additional fee.

Remark on Protest

[ ] The additional search fees were accompanied by applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO. GB 9100018 SA 43318

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 19/04/91
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Patent document cited in search report	Publication date	Patent family member(s)		Publication date
FR-A- 2085692	31-12-71	CA-A-	985626	16-03-76
		CH-A-	535050	31-03-73
		DE-A-	2110932	23-09-71
		GB-A-	1353635	22-05-74
		US-A-	3984571	05-10-76
EP-A- 0193372	03-09-86	JP-A-	61194034	28-08-86
		US-A-	4985242	15-01-91